REMARKS

I. Status of the Claims

Claims 1, 5-10, 60 and 61 are pending. No claims have been amended, added, or canceled.

II. Yang's arsenic trioxide tablet does not anticipate the presently claimed composition, which consists essentially of arsenic sulfide and a carrier

Claims 1, 5, 60 and 61 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Yang, CN 1061908. According to the Examiner, "it appears that both the prior art and instant inventions are to the treatment of cancer." Office Action at page 2.

More specifically, the Examiner reasons that the transition "consisting essentially of" does not necessarily exclude a constituent that does not materially impact on the invention. *See* Office Action at page 2. In keeping with that rationale, he further posits that "the presence of arsenic trioxide would not materially impact the invention (i.e., the invention with or without arsenic trioxide would still be effective at treating cancer and the presence of arsenic trioxide would not render the invention having some other utility)." *Id.* at page 3.

The cited Yang document is a one paragraph English translation of the CN 1061908 abstract. The substance of Yang is as follows:

> A process for manufacturing an anticancer drug to treat the early-stage cervical cancer or skin cancer involving: mixing and heating pulverized arsenic trioxide 30-75, realgar 2-8, alunite 40-100, and Commiphora myrrh resin, cooling, and then pressing that mixture into a tablet.

(Emphasis added.)

Thus, Yang's anticancer drug contains four ingredients: (1) arsenic trioxide, (2) realgar, (3) alunite, a mineral used in making alum, and (4) resin from the plant, *Commiphora myrrh*. From the stated respective quantities of these substances, it is apparent that arsenic trioxide (~41%) and alunite (~55%) make up approximately 96% of the final

tablet. The remaining 4% presumably contains the impure realgar ore and enough resin to bind the mixture together.

Accordingly, it is reasonable to presume that Yang recognized arsenic trioxide to be a primary anticancer agent, which is consistent with the conventional wisdom at that time. Please see Applicants' remarks at page 7 of their paper filed on January 11, 2005, where they discussed the conventional perception that arsenic sulfide was a poison but arsenic trioxide had anticancer properties.

In the same vein, Applicants would call the Examiner's attention to Waxman & Anderson, "History of the development of arsenic derivatives in cancer therapy," *Oncologist*, 6 Suppl. 2: 3-10, 2001 (appended). Waxman is a review article that corroborates Applicants' stated position that arsenic trioxide has been deemed the primary arsenic anticancer agent in this context. Indeed, Waxman relates that realgar *is* arsenic sulfide and is colloquially known as "red arsenic." Red arsenic is "toxic" and a chemically unstable complex sulfide. See the Introduction at page 3. Red arsenic is distinct from "white arsenic," which is arsenic trioxide. Arsenic trioxide is "an industrial by-product produced by roasting . . . realgar" and is "often more stable" and "less toxic" than red arsenic. *Id.* Waxman documents in exacting terms the historical use of arsenic trioxide as an anticancer agent, from Hippocrates to the present day.

As Waxman evidences, arsenic sulfide was never perceived as an anticancer agent, primarily because, as Applicants have stressed, it was a well-established poison. Contrary to the Examiner's position, therefore, arsenic trioxide *would* be expected to impact materially on the presently claimed invention.

The Examiner also seems to equate the recited "arsenic sulfide compound" with Yang's realgar, and implies that Yang's independent addition of arsenic trioxide somehow is equivalent to whatever trace amounts of arsenic trioxide, if any, in that realgar/"arsenic sulfide compound." By the Examiner's rationale, in other words, Yang is anticipatory art because it teaches a carrier plus arsenic sulfide compound, *i.e.*, realgar.

Yet, the Examiner cannot reasonably dismiss the fact that almost half of Yang's tablet is made up of arsenic trioxide. Indeed, Yang's tablet is primarily an arsenic *trioxide*

compound, not an "arsenic *sulfide* compound" as presently claimed. Thus, Yang does *not* suggest, let alone teach, a composition that "consists essentially of" an arsenic sulfide compound and a carrier. Yang teaches a method for producing a tablet, which can be presumed to contain primarily arsenic trioxide and alunite.

The Examiner previously recognized this distinction. At page 3 of the office action dated June 2, 2005, he reasoned that, since Applicants "add arsenic trioxide in dependent claims" 56-59, now canceled, then claim 1 does not exclude arsenic trioxide; hence, Yang applies. Applicants had added claims 56-59 to recite the level of purity of the claimed arsenic sulfide compound (*i.e.*, it contained less than 0.1% arsenic trioxide), but they decided to cancel those claims, purely to expedite prosecution, in keeping with the Examiner's own line of thinking. The Examiner also told Applicants by phone that "consists essentially of" with respect to the Yang reference would be construed to exclude the presence of arsenic trioxide in the arsenic sulfide compound. Please see page 5 of Applicants' paper dated January 11, 2005, and page 5 of their paper dated September 1, 2005.

The present Section 102(b) rejection over Yang, therefore, is at odds with the course of prosecution to date. Despite the present, unexplained divergence from that course, and for the reasons proffered above, Applicants maintain that Yang does ***not*** anticipate a formulation of an arsenic sulfide compound composition that contains a carrier.

Simply put, Yang does not contemplate a method of making an arsenic-formulated tablet that excludes arsenic trioxide. Applicants have maintained throughout prosecution that the claimed arsenic sulfide compound is a purified form of realgar that is substantially free of impurities, such as arsenic trioxide, which, if it is present, should be at a level that is less than 0.1%. To construe claim language, which expressly captures this notion, as reading on Yang's tablet, where the presence of about 41% of arsenic trioxide is *mandatory*, is unsupportable and improper.

Yang is not anticipatory prior art. For this reason, Applicants respectfully request that this rejection be withdrawn.

III. Ellison is not available as prior art because the claimed invention was made before Ellison's earliest effective filing date

Claims 1, 5, and 6 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Ellison (USSN 2002/0183385, which matured into U.S. Patent No. 6,875,451). According to the Examiner, "Ellison suggests that arsenic trioxide is the preferred cancer treatment agent" but this agent "does not specifically comprise arsenic trioxide." Office Action at page 4.

Ellison is not prior art under 102(e), however. Applicants establish here that the claimed invention was made before Ellison's earliest effective filing date, October 15, 1997 ("the critical date").

Before the critical date, inventor Dao-Pei Lu discussed and published his research on arsenic sulfide as an anticancer agent at a China-Korea Conference in Beijing. A colleague, Dr. Sang-We Kim, returned to Korea with the abstract booklet and thereby established communication of Dr. Lu's invention to a WTO member country.

35 U.S.C. § 104(a)(1) ("Invention made abroad") states:

> *In proceedings in the Patent and Trademark Office, in the courts, and before any other competent authority, an applicant for a patent, or a patentee, may not establish a date of invention by reference to knowledge or use thereof, or other activity with respect thereto, in a foreign country other than a NAFTA country or a WTO member country, except as provided in sections 119 and 365 of this title.*

With this response, Applicants submit the declaration under 37 C.F.R. § 1.131 of Sang-We Kim, who attests to this course of events and corroborates a date of invention for the presently claimed subject matter in Korea, a WTO member country.

Importantly, Dr. Kim also testifies that by July 9, 1997, "it was common knowledge throughout Asia that 'realgar' and 'arsenic sulfide' were interchangeable terms. It was well accepted, in China for example, that realgar was a more widely-used *designation* for arsenic sulfide." Kim declaration at paragraph 5 (emphasis added). Thus, when Dr. Lu gave his presentation and when Dr. Kim read the accompanying abstract, Dr. Kim "understood that Dr. Lu's study . . . described the effects of arsenic sulfide to treat hematological cancer." *Id.*

In other words, Dr. Kim was not under the impression that Dr. Lu's arsenic sulfide compound was anything other than arsenic sulfide. Furthermore, he testifies that realgar is a colloquial term for arsenic disulfide, its more precise and chemically accurate name.

Informed by Dr. Lu's presentation and carrying a copy of Dr. Lu's abstract, Dr. Kim traveled to Korea after the conference ended on July 10, 1997. Accordingly, Dr. Lu's invention effectively was introduced into a WTO country by July 10th, thereby establishing a date of invention that is before the Ellison critical date. By the same token, Applicants have removed Ellison as citable prior art, obviating the Section 102(e) rejection at issue.

IV. Claims 7 and 8 are not obvious in light of Yang because the prior art taught away from using arsenic sulfide and because there was no motivation to use the recited amounts of arsenic sulfide in Yang's arsenic trioxide composition

Claims 7 and 8 stand rejected under 35 U.S.C. § 103(a) over Yang, *supra*. According to the Examiner, Yang "teaches all that is recited in claims 7 and 8 except for the composition comprising As4S4 [claim 7] or 100 mg to 2 g of arsenic sulfide [claim 8]." Office Action at page 5.

These qualifications notwithstanding, the Examiner considers the claimed subject matter to be obvious, within the meaning of Section 103, because (a) one of ordinary skill would have expected other arsenic compounds, such as As_4S_4, to be effective in cancer treatment and (b) it would have been obvious to determine the optimum amount of arsenic sulfide. As to point (b), the Examiner believes that the skilled person would have been motivated to make a "effective and safe" composition for cancer treatment: "it is very possible that the safe and effective amount of arsenic sulfide at the time of Yang's invention would have fallen within the range of arsenic 100 mg to 2 g disclosed in the instant invention." Office Action at page 6.

At the outset, it would not have been obvious at the time the present application was filed that arsenic sulfide, regardless of isomeric composition, was an effective anticancer agent. As Applicants have endeavored to explain, arsenic *trioxide* was the perceived anticancer agent at the time. The arsenic *sulfides* were deemed poisonous. Thus, the skilled person would not have made the extrapolation from trioxide to sulfide as an effective cancer

treatment, let alone would have made any prediction concerning the fungibility between As_2S_2 and As_4S_4.

Contrary to the Examiner's position, the skilled person was under the assumption, which prevailed throughout conventional wisdom, that arsenic sulfide was toxic and unstable. On the other hand, the skilled person knew that arsenic trioxide was a "safe and effective" anticancer agent. To the skilled person, therefore, the "optimum" amount of arsenic sulfide would have been at a level that would not harm the patient. Conversely, the optimum amount of arsenic trioxide would have been any amount that would help to cure the patient. If he had been so inclined, therefore, Yang would have optimized the amount of poisonous realgar/arsenic sulfide to prevent harm. That rationale is in stark opposition to the optimization that the Examiner posits; *i.e.*, an "optimization" necessary for formulating the presently claimed composition. That is, the arsenic sulfide of the present invention would be optimized to help cure the patient, akin to Yang's use of approximately 41% **trioxide** in his tablet.

The Examiner engages in pure speculation when he conjectures that "it is very possible that the safe and effective amount of arsenic sulfide at the time of Yang's invention would have fallen within the range of arsenic 100 mg to 2 g disclosed in the instant invention." To the contrary, the range for optimizing arsenic sulfide would have been different for the dosage range for arsenic trioxide, for the reasons given above.

Yang's single paragraph disclosure doesn't even recite units of molecular weight after each ingredient, *e.g.*, "arsenic trioxide 30-75." Moreover, even if Yang did include appropriate milligram units, the skilled artisan would not have been motivated to exceed the range, given by Yang, for using realgar, "2-8." Yang provides the acceptable amount of realgar: 2-8. Nothing in Yang would have suggested to the skilled person that, actually, he could replace "2-8" amounts of realgar with "100 mg to 2 g" as recited in claim 8.

Lastly, the Examiner employs impermissible hindsight reconstruction, based on Applicants' own disclosure, to arrive at an acceptable range of realgar. Without the subject matter of claim 8, the Examiner could not possibly have identified the arsenic sulfide range of

"100 mg to 2 g" from Yang's disclosure. Accordingly, Yang does not render claims 7 and 8 as unpatentable. Applicants respectfully request that this rejection be withdrawn.

V. Ellison is not available as prior art and therefore the obviousness rejection based on Ellison is moot

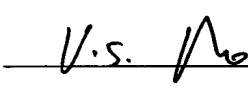
Claims 1, 5-8, 60, and 61 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Ellison, *supra*. For the reasons outlined above, Ellison is not available as prior art, and this rejection should be withdrawn.

CONCLUSION

Applicants believe that this application is in condition for allowance. Applicants invite the Examiner to contact the undersigned if that would help to expedite prosecution and allowance.

Respectfully submitted,

Date May 31, 2006

By 

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